A SAFETY AND FEASIBILITY STUDY OF ACTIVE IMMUNOTHERAPY IN PATIENTS WITH METASTATIC PROSTATE CARCINOMA USING AUTOLOGOUS DENDRITIC CELLS PULSED WITH RNA ENCODING PROSTATE SPECIFIC ANTIGEN, PSA.

SCIENTIFIC ABSTRACT

The objective of this safety and feasibility study is to develop a clinically relevant and broadly applicable vaccine strategy for the treatment of patients with advanced prostate cancer. In particular, we propose to study the use of autologous dendritic cells (DC) transfected with RNA encoding PSA ($DC_{PSA\text{-}RNA}$) for their ability to induce significant levels of PSA specific T cells in prostate cancer patients.

A large body of preclinical studies has shown that vaccinations with RNA transfected dendritic cells can serve as a potent and widely applicable platform to elicit tumor specific T cell responses in cancer patients. Furthermore, we have demonstrated that PSA-RNA transfected DC generated from prostate cancer patients can induce potent PSA responses *in vitro* regardless of the cellular MHC composition, a fact which will greatly expand the patient population eligible for this broadly applicable therapy. This immune response is ultimately hoped to reduce tumor burden and to prolong survival of prostate cancer patients

PSA-RNA will provide us with a universal, well-defined reagent in the form of PSA antigens that can be generated, characterized and stored using simple and inexpensive established procedures. RNA molecules are transitory in nature and RNA transcripts do not integrate into chromosomal DNA, thereby eliminating or greatly reducing the risks of insertional mutagenesis in eukaryotic cells.

The overall objective of this safety and feasibility trial is to evaluate this modality with respect to safety of clinical administration and induction of PSA specific T cell responses. Escalating doses of autologous progenitor derived DC transfected with PSA–RNA will be administered in dose ranges feasible from a single leukapheresis procedure. The primary and secondary objectives of this study are:

a) Evaluate the safety and feasibility of escalated doses of $DC_{TU\text{-}RNA}$.

b) Evaluate the induction of tumor specific immune responses following $DC_{TU\text{-}RNA}$ administration.

c) Monitor eventual clinical responses as evidenced by biochemical or measurable disease response criteria.

d) Develop a DC vaccination platform for patients with advanced or recurrent prostate cancer.

It is hoped that this trial will set the stage for definitive trials designed to demonstrate a clinical benefit of active immunotherapy in prostate cancer patients using tumor RNA transfected DC vaccines by reducing cancer recurrence and metastasis.